CLAIMS

1. A polypeptide comprising an amino acid sequence having homology of at least 90% to any one of the polypeptides described in the following (A) to (L), or a salt thereof:

(A) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 2, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 1;

(B) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 2 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 1 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element;

(C) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 4, or a polypeptide comprising an amino acid sequence encoded by cDNA capable

of hybridizing to the nucleotide sequence represented by SEQ ID NO: 3;

(D) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 4 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 3 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element;

(E) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 6, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 5;

(F) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 6 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 5 and having activity of regulating the

transcription of a gene that is under the control of a cAMP responsive element;

(G) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 8, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 7;

(H) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 8 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 7 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element;

(I) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 10, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 9;

(J) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid

sequence represented by SEQ ID NO: 10 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 9 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element;

(K) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 12, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 11; and

(L) a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 12 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element, or a polypeptide comprising an amino acid sequence encoded by cDNA capable of hybridizing to the nucleotide sequence represented by SEQ ID NO: 11 and having activity of regulating the transcription of a gene that is under the control of a cAMP responsive element.

2. The polypeptide according to claim 1, or a salt

thereof, which is obtained by separating and purifying from warm-blooded animal cells.

3. The polypeptide according to claim 2, or a salt thereof, wherein the animal cells are derived from a mouse.

4. A polynucleotide comprising a nucleotide sequence having homology of at least 95% to any one of the polynucleotides described in the following (a) to (m):

(a) a polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 1, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 1;

(b) a polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 3, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 3;

(c) a polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 5, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 5;

(d) a polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 7, or a polynucleotide that

is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 7;

(e) a polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 9, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 9;

(f) a polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 11, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence represented by SEQ ID NO: 11;

(g) a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 2, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence encoding the polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 2;

(h) a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 4, or a polynucleotide

that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence encoding the polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 4;

(i) a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 6, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence encoding the polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 6;

(j) a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 8, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence encoding the polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 8;

(k) a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid

sequence represented by SEQ ID NO: 10, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence encoding the polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 10;

(l) a polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 12, or a polynucleotide that is cDNA capable of hybridizing to the polynucleotide comprising the nucleotide sequence encoding the polypeptide comprising an amino acid sequence identical to or substantially identical to the amino acid sequence represented by SEQ ID NO: 12; and

(m) a polynucleotide capable of hybridizing to any one of the polynucleotides described in (a) to (l) above under stringent conditions.

5. A recombinant vector comprising a polynucleotide as recited in claim 4.

6. An expression vector comprising a the polynucleotide as recited in claim 4.

7. Host cells harboring an expression vector as recited

in claim 6.

8. A method for producing a polypeptide or a salt thereof as recited in claim 1, which comprises culturing a host cell as recited in claim 7 under conditions that are suitable for the expression of the polypeptide, and recovering the polypeptide from the culture product obtained.

9. The method for producing a polypeptide or a salt thereof according to claim 8, wherein the culture of the host cell is carried out in the presence of a substance having an action to induce fat differentiation.

10. A method for producing a polypeptide or a salt thereof according to claim 1, which comprises culturing precursor fat cells in the presence of a substance having an action to induce fat differentiation, and recovering the polypeptide as recited in claim 1 or a salt thereof from the culture product obtained.

11. A polypeptide or a salt thereof produced by a method for producing a polypeptide or a salt thereof as recited in any one of claims 8 to 10.

12. A nucleic acid probe, which is useful for detecting

a polynucleotide as recited in claim 4 or a polynucleotide encoding a polypeptide as recited in claim 1.

13. An antibody having an affinity for the polypeptide as recited in claim 1 or a fragment thereof.

14. A hybridoma capable of generating an antibody having an affinity for the polypeptide as recited in claim 1.

15. A pharmaceutical composition, which comprises the polypeptide as recited in claim 1 or the recombinant vector as recited in claim 5.

16. The pharmaceutical composition according to claim 15, which further comprises a substance having an action to induce fat differentiation.

17. The pharmaceutical composition according to claim 15 or 16, which is used as an agent for preventing or improving a disease with which the differentiation of fat cells or an increase in the function of glucose or lipid metabolism is associated.

18. The pharmaceutical composition according to claim 15 or 16, wherein the disease is diabetes, adiposis, hyperlipidemia, hypertension, arteriosclerosis,

hyperuricemia, or a cardiovascular disease.

19. A composition for use in gene diagnosis, which comprises a polynucleotide as recited in claim 4.

20. The composition for use in gene diagnosis according to claim 19, which detects the expression of DNA or mRNA encoding salt-inducible kinase 2.

21. The composition for use in gene diagnosis according to claim 19, which is used for diagnosis of a disease with which the differentiation of fat cells or the disorder of function of glucose or lipid metabolism is associated.

22. The composition for use in gene diagnosis according to claim 21, wherein the disease is diabetes, adiposis, hyperlipidemia, hypertension, arteriosclerosis, hyperuricemia, or a cardiovascular disease.

23. A pharmaceutical composition, which comprises an antibody as recited in claim 13, a fragment thereof, or an antisense nucleotide complementarily binding to a polynucleotide as recited in claim 4.

24. The pharmaceutical composition according to claim 23, which is used as an agent for preventing or improving

a disease with which the differentiation of fat cells or glucose or lipid metabolism is associated.

25. The pharmaceutical composition according to claim 23, wherein the disease is diabetes, adiposis, hyperlipidemia, hypertension, arteriosclerosis, hyperuricemia, or a cardiovascular disease.

26. The pharmaceutical composition according to claim 23, which is used for diagnosis of a disease with which the suppression of the differentiation of fat cells or the disorder of the metabolic function thereof is associated.

27. The pharmaceutical composition according to claim 23, wherein the disease is diabetes, adiposis, hyperlipidemia, hypertension, arteriosclerosis, hyperuricemia, or a cardiovascular disease.

28. A method for preventing or improving a disease or physiological condition which is developed by a decrease in the expression of salt-inducible kinase 2, characterized in that the method comprises administration of a pharmaceutical composition as recited in claim 15 or 16.

29. The method for preventing or improving a disease or physiological condition according to claim 28, wherein the disease or physiological condition involves the disorder of glucose metabolism, the disorder of lipid metabolism, or cranial nerve injury.

30. A method for preventing or improving a disease or physiological condition which is developed by an increase in the expression of salt-inducible kinase 2, characterized in that the method comprises administration of a pharmaceutical composition as recited in claim 23.

31. The method for preventing or improving a disease or physiological condition according to claim 30, wherein the disease or physiological condition involves the disorder of glucose metabolism, the disorder of lipid metabolism, or cranial nerve injury.

32. A method for screening a compound capable of promoting or inhibiting the activity of a polypeptide as recited in claim 1, comprising the steps of: allowing an analyte comprising a polypeptide as recited in claim 1 to come into contact with a test compound; and detecting an activity of promoting or inhibiting the activity of the polypeptide as recited in claim 1.

33. The screening method according to claim 32, which detects the activity of promoting or inhibiting the activity of the polypeptide as recited in claim 1, using the auto-phosphorylating activity of the polypeptide as recited in claim 1 and/or the activity thereof of phosphorylating other proteins as an indicator.

34. A method for screening a compound capable of promoting or inhibiting the activity of a polypeptide as recited in claim 1, the method comprising steps of: allowing an expression vector comprising a polynucleotide as recited in claim 4 and a reporter gene that is under the control of a cAMP responsive element to come into contact with a test compound; and detecting an activity of promoting or inhibiting the activity of the polypeptide as recited in claim 1.

35. A method for screening a compound specifically binding to a polypeptide as recited in claim 1, comprising steps of: allowing a polypeptide as recited in claim 1 to come into contact with a test compound; and detecting the binding of the test compound with the polypeptide, thereby identifying a compound specifically binding to the polypeptide.

36. A method for screening a compound having an ability

to regulate the activity of a polypeptide as recited in claim 1, the method comprising steps of: allowing a polypeptide as recited in claim 1 to come into contact with a test compound under conditions where the polypeptide exhibits its activity; evaluating the activity of the polypeptide in the presence of the test compound; comparing the thus evaluated activity with the activity of the polypeptide in the absence of the test compound; and identifying the ability of the test compound to regulate the activity of the polypeptide based on the comparison results.

37. A method for screening a compound having effects on the expression of a polynucleotide as recited in claim 4, the method comprising steps of: allowing a target polynucleotide analyte comprising a polynucleotide as recited in claim 4 to come into contact with a test compound under conditions that are suitable for the expression of the target polynucleotide; detecting a change in the expression of the target nucleotide; and comparing the expression of the target polynucleotide in the absence of the test compound and in the presence of various amounts of the test compounds.

38. The method for screening a compound according to any one of claims 32 to 37, which is carried out in the

presence of a substance having an action to induce fat differentiation.

39. A method for screening a compound capable of promoting or inhibiting the activity of a protein having an auto-phosphorylation ability, comprising:

a phosphorylating step of phosphorylating a protein having auto-phosphorylation ability in the presence of a test compound;

an antibody-binding step of allowing an antibody recognizing an auto-phosphorylated portion of the protein that is in a state where it has been phosphorylated or has not been phosphorylated, to react with the protein; and

a measuring step of measuring the reaction of the protein with the antibody.

40. A method for screening a compound capable of promoting or inhibiting the activity of salt-inducible kinase, comprising:

a phosphorylating step of phosphorylating salt-inducible kinase in the presence of a test compound;

an antibody-binding step of allowing an antibody recognizing an auto-phosphorylated portion of the salt-inducible kinase that is in a state where it has been phosphorylated or has not been phosphorylated, to react

with the salt-inducible kinase; and

a measuring step of measuring the reaction of the salt-inducible kinase with the antibody.

41. A method for screening a compound capable of promoting or inhibiting the activity of the polypeptide according to claim 1, comprising:

a phosphorylating step of phosphorylating a peptide as recited in claim 1 in the presence of a test compound;

an antibody-binding step of allowing an antibody recognizing an auto-phosphorylated portion of the polypeptide that is in a state where it has been phosphorylated or has not been phosphorylated, to react with the polypeptide; and

a measuring step of measuring the reaction of the polypeptide with the antibody.

42. The screening method according to claim 39, wherein cells having an ability to generate a protein having an auto-phosphorylation ability or host cells transformed with an expression vector comprising such a protein having an auto-phosphorylation ability are cultured under conditions that are suitable for the expression of a protein, and a polypeptide obtained from the obtained culture product is used as a protein having an auto-phosphorylation ability.

43. The screening method according to claim 40, wherein cells having an ability to generate salt-inducible kinase or host cells transformed with the expression vector as recited in claim 6 are cultured under conditions that are suitable for the expression of a polypeptide, and a polypeptide obtained from the obtained culture product is used as salt-inducible kinase.

44. The screening method according to claim 41, wherein host cells transformed with an expression vector as recited in claim 6 are cultured under conditions that are suitable for the expression of a polypeptide, and a polypeptide obtained from the obtained culture product is used as the polypeptide or a salt thereof.

45. The screening method according to any one of claims 39 to 44, which is carried out in the presence of a substance having an action to induce fat differentiation.

46. A method for screening a compound capable of promoting or inhibiting the activity of a protein having an auto-phosphorylation ability, comprising:

a step of culturing cells having an ability to generate a protein having an auto-phosphorylation ability in the presence of a test compound under conditions that

are suitable for the expression of the protein;

an antibody-binding step of allowing the cells to come into contact with an antibody recognizing an auto-phosphorylated portion of the protein that is in a state where it has been phosphorylated or has not been phosphorylated, so as to allow the protein to react with the antibody; and

a measuring step of detecting the reaction of the protein with the antibody.

47. The screening method according to claim 46, wherein the culture of the cells is carried out in the presence of a substance having an action to induce fat differentiation.

48. A method for screening a compound capable of promoting or inhibiting the activity of salt-inducible kinase, comprising:

a step of culturing cells having an ability to generate salt-inducible kinase in the presence of a test compound under conditions that are suitable for the expression of salt-inducible kinase;

an antibody-binding step of allowing the cells to come into contact with an antibody recognizing an auto-phosphorylated portion of the salt-inducible kinase that is in a state where it has been phosphorylated or

has not been phosphorylated, so as to allow the salt-inducible kinase to react with the antibody; and

a measuring step of detecting the reaction of the salt-inducible kinase with the antibody.

49. The screening method according to claim 48, wherein the culture of the cells is carried out in the presence of a substance having an action to induce fat differentiation.

50. A method for screening a compound capable of promoting or inhibiting the activity of a polypeptide comprising:

a step of culturing host cells harboring a recombinant vector comprising a polynucleotide as recited in claim 4 in the presence of a test compound under conditions that are suitable for the expression of a polypeptide;

an antibody-binding step of allowing the host cells to come into contact with an antibody recognizing an auto-phosphorylated portion of the polypeptide that is in a state where it has been phosphorylated or has not been phosphorylated, so as to allow the polypeptide to react with the antibody; and

a measuring step of detecting the reaction of the polypeptide with the antibody.

51. The screening method according to claim 50, wherein the culture of the cells is carried out in the presence of a substance having an action to induce fat differentiation.

52. A method for screening a compound capable of promoting or inhibiting the activity of salt-inducible kinase, comprising:

a phosphorylating step of allowing salt-inducible kinase to come into contact with a substrate that is to be phosphorylated with the salt-inducible kinase in the presence of a test compound, so as to phosphorylate the substrate;

an antibody-binding step of allowing an antibody recognizing a substrate that is in a state where it has been phosphorylated or has not been phosphorylated, to react with the substrate; and

a measuring step of detecting the reaction of the substrate with the antibody.

53. A pharmaceutical composition, which comprises the compound capable of promoting or inhibiting the activity of a polypeptide as recited in claim 1, which is identified by a screening method as recited in any one of claims 32 to 52.

54. The screening method according to any one of claims 32 to 52, which screens for a compound used for preventing or treating diabetes, adiposis, hyperlipidemia, hypertension, arteriosclerosis, hyperuricemia, or a cardiovascular disease.

55. A kit for screening a compound capable of promoting or inhibiting the activity of the polypeptide according to claim 1, comprising a polypeptide as recited in claim 1.

56. The screening kit according to claim 55, which comprises a polypeptide as recited in claim 1 or a phosphate group donor that phosphorylates other substrates.

57. The screening kit according to claim 55 or 56, which comprises a substrate polypeptide that is phosphorylated by a polypeptide as recited in claim 1.

58. A kit for screening a compound capable of promoting or inhibiting a polypeptide as recited in claim 1, comprising host cells transformed with an expression vector as recited in claim 6.

59. The screening kit according to claim 58, which

comprises a medium used for the host cells and a reagent for activating a cAMP responsive element.

60. The screening kit according to any one of claims 55 to 59, which comprises a substance having an action to induce fat differentiation.

61. A kit for screening a compound capable of promoting or inhibiting the activity of a protein having an auto-phosphorylation ability, comprising a protein having an auto-phosphorylation ability and an antibody recognizing an auto-phosphorylated portion of the protein that is in a state where it has been phosphorylated or has not been phosphorylated.

62. A kit for screening a compound capable of promoting or inhibiting the activity of salt-inducible kinase, comprising salt-inducible kinase and an antibody recognizing an auto-phosphorylated portion of the salt-inducible kinase that is in a state where it has been phosphorylated or has not been phosphorylated.

63. A kit for screening a compound capable of promoting or inhibiting the activity of the polypeptide according to claim 1, comprising a polypeptide as recited in claim 1 and an antibody recognizing an auto-phosphorylated

portion of the polypeptide that is in a state where it has been phosphorylated or has not been phosphorylated.

64. A kit for screening a compound capable of promoting or inhibiting the activity of a protein having an auto-phosphorylation ability, comprising cells having an ability to generate a protein having an auto-phosphorylation ability and an antibody recognizing an auto-phosphorylated portion of the protein that is in a state where it has been phosphorylated or has not been phosphorylated.

65. A kit for screening a compound capable of promoting or inhibiting the activity of a protein having an auto-phosphorylation ability, comprising cells having an ability to generate salt-inducible kinase and an antibody recognizing an auto-phosphorylated portion of the salt-inducible kinase that is in a state where it has been phosphorylated or has not been phosphorylated.

66. A kit for screening a compound capable of promoting or inhibiting the activity of a protein having an auto-phosphorylation ability, comprising host cells harboring a recombinant vector comprising the polynucleotide as recited in claim 4 and an antibody recognizing an auto-phosphorylated portion of a protein

that is in a state where it has been phosphorylated or has not been phosphorylated.

67. A kit for screening a compound capable of promoting or inhibiting the activity of salt-inducible kinase, comprising host cells harboring a recombinant vector comprising a polynucleotide as recited in claim 4 and an antibody recognizing an auto-phosphorylated portion of salt-inducible kinase that is in a state where it has been phosphorylated or has not been phosphorylated.

68. A kit for screening a compound capable of promoting or inhibiting the activity of the polypeptide according to claim 1, comprising host cells harboring a recombinant vector comprising a polynucleotide as recited in claim 4 and an antibody recognizing a polypeptide as recited in claim 1 that is in a state where it has been phosphorylated or has not been phosphorylated.

69. The screening kit according to any one of claims 61 to 68, which comprises a substance having an action to induce fat differentiation.

70. A method for screening a compound capable of promoting or inhibiting the induction of a polypeptide as recited in claim 1, comprising a step of detecting the

activity of promoting or inhibiting the induction of a polypeptide as recited in claim 1, using, as an indicator, mRNA encoding the polypeptide as recited in claim 1, the auto-phosphorylating activity of the polypeptide as recited in claim 1 and/or the activity thereof of phosphorylating other proteins, or the activity of regulating the transcription of a gene that is under the control of a cAMP responsive element.